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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,091	11/25/2003	Jose Remacle	4044.001	7897

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,091	REMACLE ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/7/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-9,13-15 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-5, 7-9, 13-15 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/7/09 has been entered.

Status of Claims

Claims 1, 4-5, 7-9, 13-15 and 17-22 are pending and under examination.

Claims 2-3, 6, 10-12 and 16 have been cancelled.

Withdrawn Objections/Rejections

In view of applicants' amendments to the claims and arguments, the objection to claim 6; the 35 USC 112, second paragraph and the 35 USC 103 rejections in view of Guo are withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC S 103

Claims 1, 4-5, 7-9, 13-15 and 17-22, as amended and added, are rejected under 35 U.S.C. 103(a) as being unpatentable over either Stillman (20030175827) or Decker(GB 2,016,687A) in combination with either Sandford (US 2003/0134294) or Moreadith et al(USP 6632934)and Schultz et al(20040198637).

Stillman discloses throughout the patent at e.g., paragraphs [0010]-[0011]:

> …[A] method for producing a thin film dried protein composition comprising making a protein containing solution that is to be dried on a surface, preferably a biologically active protein. The term "biologically active" includes any protein that can participate in a specific binding reaction, (such as antibodies, antibody fragments, antigens, antigen fragments)(capture proteins, as claimed), as well as peptides or enzymes.) The solution is made with a buffer that maintains the surface pH between about 5.0 and 9.0 during solution **drying and with a saccharide in an amount sufficient to stabilize the protein during solution drying.** The solution is then applied to a support having the surface for depositing. Thin film of protein containing solution is allowed to **dry on the support surface under normal pressures.**

Stillman further discloses throughout the patent at e.g., paragraph [0026], referring to FIG. 3:

> A series of compositions were tested including .... antibody protein. The difference amongst the solutions was the saccharide used, namely, glucose, mannitol, xylose, trehalose, maltodextrin, and glucuronic acid. **Spotted and**

dried solution spots were tested for shelf life, i.e., the retention of biological activity, in this case, a specific binding reaction…...

Decker discloses throughout the article at e.g., pages 2 up to 5, an immunoassay method for the detection and determination of antigens and antibodies. The method comprises an indirect application of an antibody or antigen to a solid support. It generally involves the procedure in which the solid support is precoated with antigen or antibody to potentiate the adherence of the antibody or antigen. The reagents consist of a solid support that has been coated either directly or indirectly with an antigen or antibody and stabilized with a sugar coating to impart a storage capability. The percent of sugar e.g., xylitol, mannitol and sorbitol is given in Table II.

Each of Stillman and Decker does not disclose the use of antiseptic as sodium azide and that the protein is covalently linked to the solid support and the protein having at least 70% activity after six months of storage at 0-8 degrees or 15-30 degrees.

Sandford discloses at paragraph [0197] that preservatives like azide are effective to retard or prevent microbial proliferation. Sandford discloses at paragraph [0199] that lyoprotectants are effective to reduce or prevent chemical or

physical instability of a protein upon lyophilization and storage. Examples of a polyol are trihydric or higher sugar alcohol (e.g., glycerin, erythritol, glycerol, arabitol, xylitol, sorbitol, and mannitol). Sandford also discloses the use of borate buffer.

Schultz et al discloses throughout the patent at e.g., paragraph [0048]:

Systems for immobilizing polypeptides on a solid support, as well as the resulting solid supports containing the polypeptides, e.g., protein arrays…. **The systems allow one to covalently or non-covalently attach the polypeptides to the solid support in such a manner as to preserve the function of the polypeptides or to regain their functionality once attached. The covalent or non- covalent attachment generally does not substantially affect the structure, function, or activity of the polypeptide (e.g., catalytic activity, ability to bind other polypeptides, ability to bind nucleic acids, ability to bind small molecules, 3-D structure, etc.).** The protein arrays…..are versatile and can be adapted to a variety of protein analysis formats.

Moreadith discloses throughout the patent at e.g., col. 24, lines 23-35:

..In general, due to the relative stability of peptides, they may be readily stored in aqueous solutions for fairly long periods of time if desired, e.g., up to six months or more, in virtually any aqueous solution without appreciable degradation or loss of antigenic activity. However, where extended aqueous storage is contemplated it will generally be desirable to include agents including buffer…..to maintain a pH of about 7.0 to about 7.5. Moreover, it may be desirable to include agents which will inhibit microbial growth, such as sodium azide…. For extended storage in an aqueous state it will be desirable to store the solutions at about 4.degree. C., or more preferably, frozen. Of course, where the peptides are stored in a lyophilized or powdered state, they may be stored virtually indefinitely,

e.g., in metered aliquots that may be rehydrated with a predetermined amount of water (preferably distilled) or buffer prior to use.

Moreadith further discloses at e.g., col. 42, lines 30-40, that the term substantially purified refers to a composition in which the protein or peptide forms the major component of the composition, such as constituting about 50%, about 60%, about 70%, about 80%, about 90%, about 95% or more of the proteins in the composition.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use azide in the method of either Decker or Stillman as taught by either Sandford or Moreadith. The advantages taught by Sandford would provide the motivation to one having ordinary skill in the art as to the known use of azide as a preservative. Furthermore, as taught by Moreadith, sodium azide inhibits microbial growth as such the protein can be stored for an indefinite time of up to six months. The use of azide as a preservative is predictable from the teachings of both Sandford and Moreadith which teaches the conventionality of sodium azide as microbial inhibitor. It would be within the ordinary skill in the art at the time the invention was made to pick the specific saccharide within those taught by Decker or

Stillman. Furthermore, as taught by Schultz the protein can be covalently or non-covalently link to the array in a manner that preserves its function.

Response to Arguments

(Please note that the arguments below have been modified to address the new and amended claims.)

Applicants submit that the cited references, alone or in combination, fail to disclose or suggest every element of the present claims. For example, Stillman and Decker fail to disclose or suggest allowing the spotted solution to dry on the support and storing the micro-array between 0 and 8°C or between 15 and 30°C, wherein all said captured proteins have at least 70% of their activity after 6 months of storage as required, in part, by independent Claims 1 and 21. By contrast, Stillman teaches drying spotted micro-arrays at 37°C for up to 120 days. See, Stillman, page 3, [0027]. Stillman further teaches that by using such a temperature, one can extrapolate anticipated shelf life for a dried protein composition. Id. As such, Stillman does not teach or suggest any storage temperature below 37°C or any storage time approaching the 6 months recited in the claims. Decker is similarly deficient because it never teaches or suggests storage times of 6 months or the 70%

activity of captured proteins as required, in part, by the claims.

In response, one cannot show non-obviousness by attacking the references individually where the rejection is based on a combination of references. In re Young, 159 USPQ 725 (CCPA 1968). The test for obviousness under 35 USC 103 is not the express suggestion of the claimed invention in any or all of the references but what the references taken collectively would suggest; and inferences which one skilled it in the art would reasonably be expected to drawn from the disclosure in the references. In re Preda, 159 USPQ 342 and In re Conrad, 169 USPQ 170. Thus, while Stillman or Decker does not teach storage stability of up to 6 months, Moreadith does. See the teachings of Moreadith above.

Applicants submit that the secondary references, Sandford and Schultz fail to remedy all the deficiencies of the above references. (The arguments with respect to Guo are moot as the rejection has been dropped.)

Sandford is deficient because it does not even disclose or suggest use of a micro-array maintained in dry conditions as required by the claims. Instead, Sandford teaches use of an aqueous array through the preparation of a polyurethane-hydrogel composition. See, Sandford,

Abstract. As a result, Sandford inherently fails to disclose or suggest allowing a spotted solution to dry on a solid support or the subsequent storage conditions recited in the claims. By being directed to a wet array, Sandford clearly fails to remedy the deficiencies of the primary references. One skilled in the art, moreover, would have no reason to combine Sandford (aqueous array) with either of Stillman or Decker (dry array) because the references are directed to clearly divergent arrays.

In reply, Sandford is not used for the purpose as argued since Stillman or Decker teaches, as applicants admitted above, the microarray in dry form. Sandford is employed for its teachings of the use of sodium azide for inhibiting microbes in the protein microarray.

Attention is drawn to Stillman at e.g., page 1, paragraph 0001]:

> …[A]…method [wherein]….a **thin film of a biologically active protein containing solution to be dried is deposited on the support surface wherein the film also contains a buffer that maintains the surface pH ..during drying under normal pressures and a saccharide in an amount sufficient to stabilize the protein while drying.** An advantage of the present invention is that one can make thin film assay devices, such as proteomic microarrays, using supports that normally would not be useful. (Emphasis supplied).

Thus, the combined teachings of Stillman or Decker with Sandford render the claim prima facie obvious at the time the invention was made. There is nothing new and unobvious in the use of the known sodium azide as an antimicrobe for a polypeptide in a microarray, as taught by Sandford.

Applicants argue that Schultz also fails to remedy the deficiencies of the primary references. In fact, the Office Action admits to relying on Schultz, not to teach of suggest any of the above deficiencies, but rather for its teaching that covalent or non-covalent linking of proteins in an array does not affect the proteins' activity. See, Office Action, page 11, lines 11-14.

In reply, as correctly stated by applicants, Schultz is employed for its teaching that the covalent or non-covalent attachment of the polypeptides to the solid support has been well-established in the art prior to applicants' invention. The combined teachings of Schultz and Decker or Stillman to covalently or non-covalently attach a polypeptide to a microarray are prima facie obvious to one having ordinary skill in the art at the time the invention was made.

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert.denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). See MPEP 2144.05.

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a **predictable**

> **variation, § 103 likely bars its patentability….** When considering obviousness of a combination of known elements, the operative question is thus "whether the improvement is more than the predictable use of prior art elements according to their established functions." KSR International Co. v. Teleflex Inc., 550 USPQ2d 1385 (2007). (Emphasis added).

Accordingly, there is nothing new, unexpected or unpredictable about the claimed method. The steps of producing a stable protein microarray using sugar at a given temperature and storage time is well known in the art at the time the invention was made as evident by the combined teachings of the prior art.

No claim is allowed.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Song et al (20040120956) teaches formulations of polypeptide that can be safely stored at temperatures of from about 2 to about 40.degree.C. and retain the biologically activity of the polypeptide for extended periods of time, thus, allowing a package label indicating that the solution can be held and/or used over a period of 6, 12, 18, 24, 36, 48, 72, or 96 hours or greater. If preserved diluent is used, such label can include use up to 1-12 months, one-half, one and a half, and/or two years.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-09510951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639